REPORT

Innovative Pandemic influenza preparedness Framework paves the way for sustainable improvements to pandemic preparedness

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ABSTRACT

The Pandemic influenza preparedness (PIP) Framework benefit sharing mechanism has been used to support the strengthening of pandemic preparedness in five countries in the WHO European Region. The support laid the foundation for sustainable influenza surveillance and response systems in the countries by strengthening influenza laboratory and surveillance capacities as well as capacities to detect and respond to outbreaks and treat patients with severe forms

of influenza. The results achieved will increase the contribution of countries in the WHO European Region to national, regional and global influenza surveillance and will help countries to be better prepared for the next influenza pandemic. The WHO Regional Office for Europe's implementation of the PIP Framework, is an example of how country commitment, sustained funding and a solid methodological approach can lead to enhanced pandemic preparedness in countries.

Keywords: INFLUENZA, PREPAREDNESS, PIP FRAMEWORK, SURVEILLANCE, LABORATORY, OUTBREAK INVESTIGATION AND RESPONSE

BACKGROUND

GLOBAL CONTEXT OF PANDEMIC PREPAREDNESS AND PIP FRAMEWORK

Influenza pandemics have occurred throughout history, causing widespread disease and deaths as well as high socioeconomic costs (1). The previous four pandemics, the most recent having occurred in 2009, are estimated collectively to have caused up to 50 million deaths, including 20–40 million attributed to the 1918 H1N1 pandemic almost one century ago. Even the relatively mild 2009 H1N1 pandemic is estimated to have caused between 150 000–580 000 deaths in population groups not usually associated with

a high risk of death due to influenza (2, 3), and a new pandemic is considered inevitable. Despite the extensive efforts made to prepare for a pandemic prior to 2009, the conclusion of the International Health Regulations (IHR) Review Committee, following the 2009 pandemic, was that "The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency" (4).

In 2014–2016, the outbreaks of Ebola and Zika further emphasized the need for substantial revisions in the way the global community prepares for and responds to epidemics and pandemics. As a consequence, significant reforms were

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implemented within WHO with the establishment of the WHO Health Emergencies Programme (WHE), which enhances WHO's operational capacity to respond to any acute public health event, whether caused by a biological, natural or manmade hazard or disaster, including pandemic influenza. The WHE support in the area of pandemic preparedness goes hand-in-hand with efforts to accelerate the implementation of the IHR (2005) core capacities (5). Moreover, the need for enhanced global action in the area of IHR (2005) and health emergency preparedness was corroborated with the adoption of the Sustainable Development Goals (SDGs) in 2015: SDG 3, target D, states the importance of "early warning, risk reduction and management of national and global health risks" (6).

An important instrument in the global efforts to strengthen preparedness for an influenza pandemic is PIP Framework (7), which was adopted by the World Health Assembly at its Sixty-fourth session in 2011. The PIP Framework is a unique partnership between WHO, Member States, industry and civil society who work together for a common goal: to improve the sharing of influenza viruses with human pandemic potential, and to ensure the equitable access of countries to vaccines and other pandemic-related supplies.

UTILIZATION OF PIP FRAMEWORK BENEFITS TO IMPROVE PANDEMIC PREPAREDNESS

The PIP Framework is based on two fundamental pillars: virus sharing and benefit sharing. The virus sharing pillar emphasizes the sharing of influenza viruses with pandemic potential by countries with the WHO Global Influenza Surveillance and Response System (GISRS) for the purpose of risk assessment, surveillance and the development of diagnostics, antivirals and vaccines.

The benefit pillar is composed of two parts: a) standard contracts, namely Standard Material Transfer Agreements, with companies and institutions that receive PIP biological materials from WHO GISRS and which, in return, guarantee WHO access to vaccines, antivirals and other supplies in a pandemic for use in countries; and b) the partnership contribution (PC) which entails annual cash payments from influenza vaccine manufacturers and other beneficiaries of PIP biological materials provided by WHO GISRS. Collectively, US\$ 28 million per year is received by WHO through this mechanism, of which 30% is reserved for the response to the next pandemic and 70% is used to strengthen pandemic preparedness as described in the global PIP PC Implementation Plan (8).

OBJECTIVE

The objective of this paper is to describe the approach taken and the achievements made in the implementation of the laboratory and surveillance component of the PIP PC Implementation Plan in the WHO European Region in the period 2014–2017. Five countries were identified as PIP PC recipient countries in the Region, namely Armenia, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan. These countries were selected based on an assessment of capacities available at the country level, including national ability to detect influenza viruses and to share data and viruses with WHO.

Through the implementation of the PIP PC, countries are supported to build laboratory and surveillance capacities that are essential to respond to a pandemic. Firstly, the capacities to detect a novel influenza virus, conduct risk assessment, implement response measures and inform vaccine composition. And secondly, the capacities to track the spread of a pandemic, identify risk groups and monitor impact and severity. This in turn will inform public health interventions such as pandemic vaccine, antivirals, appropriate clinical care and non-pharmaceutical public health measures (9). Many of these capacities are based on well-functioning systems for the detection and monitoring of influenza during the influenza season.

APPROACH

Between 2014 and 2017, the PIP PC was used to support the five PIP PC recipient countries in building capacities related to influenza surveillance, laboratory services, outbreak investigation and response and the clinical management of patients with severe forms of influenza. Capacity-building was done with a view to establishing sustainable mechanisms in the countries and obtaining synergistic effects by linking the aforementioned areas to each other where relevant. Four central principles were followed to ensure a successful implementation of the PIP PC:

1. OBTAINING HIGH-LEVEL COMMITMENT FROM THE PIP PC RECIPIENT COUNTRIES

In 2014, a high-level meeting was held in Copenhagen to mark the commencement and endorsement of the implementation of the PIP PC in the recipient countries.¹ Participants included the minister of health from one country and deputy ministers of

Implementation of the PIP PC in Kyrgyzstan started in 2015.

health or other high-level representatives from the other countries. The purpose of the meeting was to obtain high-level commitment to PIP PC implementation in the countries (10). During the meeting, the WHO Regional Director for Europe emphasized the importance of high-level engagement and country ownership as well as the central role of the national PIP focal points who were nominated to facilitate implementation in the countries.

2. DEVELOPING ANNUAL IMPLEMENTATION PLANS AND ESTABLISHING TEAMS OF EXPERTS

Since 2014, annual country-specific implementation plans have been developed in close collaboration between the PIP focal points, ministries of health, WHO country offices and the Regional Office. At the beginning of each year, the final plans were sent by the Regional Office to the ministers of health to obtain formal approval of the planned activities and to ensure continuing country commitment. Implementation in the countries was led by national PIP focal points and supported by a dedicated team of WHO staff and consultants. In order to make the best use of resources, the work was done in synergy with activities implemented by Armenia and Kyrgyzstan under Bilateral Cooperative Agreements with the United States Centers for Disease Control and Prevention.

3. APPLYING STANDARDIZED METHODOLOGIES AND BEST PRACTICE APPROACHES TO IMPLEMENTATION

As a first step towards the implementation of activities, comprehensive assessments based on standardized methodologies were conducted in the five countries to identify strengths and shortcomings in existing national systems for sentinel surveillance, laboratory capacity, outbreak investigation and response, and the clinical management of patients with severe forms of influenza. These assessments built on previous work which described the status of influenza surveillance in the Region (11). Following the system assessments, a parallel and similar implementation process was applied in each country, adapted to the national context.

Global and regional WHO surveillance assessment tools (12) were used to assess the existing influenza surveillance systems. For the purpose of optimizing sentinel influenza surveillance systems, feasibility studies were conducted to select representative sentinel sites to deliver high-quality data for influenza surveillance. Following the feasibility studies and the development of national surveillance guidelines, with adapted modules and standard operating procedures for sentinel sites, implementation took place through training in, for example, sample collection, reporting, data entry and bulletin

generation. Existing information technology platforms and data management capacities were assessed and country-tailored solutions were made by adapting software that was proven to be fit for purpose in other countries. Annual influenza meetings were held in each country to mark the start of the influenza season and to highlight new developments and mechanisms introduced through the PIP PC implementation. The meetings included representatives from human and animal health sectors and served as platforms for information exchange and intersectoral collaboration.

Based on initial laboratory assessments, capacity-building plans for each country were developed. These included mentoring in laboratory quality (13) as well as training in influenza virological techniques, both on-site and at the expert institution, Research Institute of Influenza in Saint Petersburg, Russian Federation, to enhance the ability of national influenza laboratories to detect and characterize influenza viruses. Support was also provided to procure essential laboratory supplies needed for specimen collection and influenza testing. In addition, laboratory personnel were trained and certified in the shipment of influenza viruses using the WHO Infectious Substances Shipping Training (14). The sharing of influenza viruses with WHO GISRS is a prerequisite for WHO recognition as a National Influenza Centre (15).

In the area of outbreak investigation and response, existing national guidelines were reviewed and tested through case studies to identify strengths and weaknesses. Based on this and best practice examples from other countries, the national guidelines were revised. Subsequently, country-specific training packages were developed and training of trainers provided for national members of rapid response teams with technical support from the Robert Koch Institute in Germany.

In addition, training in the clinical management of patients with severe forms of influenza was provided to specialists in infectious disease, intensive care and respiratory medicine in the five countries, using WHO's global Critical Care Training Short Course (16) programme and following the training of trainers model. These training courses led to the conclusion that national guidelines in this area needed to be updated. Consequently, national working groups were established to revise the existing guidelines with support from WHO.

4. SHARING OF EXPERIENCES BETWEEN COUNTRIES

As the five countries went through a similar process in the same time period, many opportunities for sharing experiences and lessons learned were created through numerous intercountry meetings between the five countries. Examples were the annual meetings for PIP national focal points, meetings of sentinel influenza surveillance site coordinators, an intercountry workshop to develop training materials for outbreak investigation and response, as well as intercountry training courses for laboratory experts.

ACHIEVEMENTS

Progress made in PIP PC implementation is formally measured at the global level through semi-annual qualitative reporting on PIP indicators and yearly qualitative reports from national experts and WHO staff working on PIP PC implementation. Quantitative and qualitative reports are presented twice a year at the PIP Advisory Group meetings which are attended by country representatives, WHO, industry and civil society. Furthermore, financial and technical implementation of PIP PC can be tracked on the PIP PC Implementation Portal (17).

In the WHO European Region, measurable achievements were made by all five countries during the first four years of PIP PC implementation (Table 1).

Firstly, influenza surveillance in the five countries has been improved with newly developed or revised national sentinel surveillance guidelines and sentinel surveillance systems that will allow for the collection of high-quality data on influenzalike illnesses and severe acute respiratory infections from newly established, or improved, sentinel sites. Furthermore, the electronic data management systems that have been developed allow for better management, analysis and interpretation of surveillance data, as well as for automated influenza bulletin generation. The introduction of influenza bulletins represents a new approach to the communication of scientific information relating to influenza in the five countries and it will enable more timely, targeted and explanatory information sharing with decision-makers, health care workers, communications experts and the media. These improvements also facilitate the sharing of influenza surveillance data with the European Surveillance System for publication in the Flu News Europe weekly influenza update, by the WHO Regional Office for Europe and the European Centre for Disease Prevention and Control, as well as in WHO global surveillance reports. Furthermore, the annual national influenza meetings held in each country are considered to be valuable platforms for the sharing of experience between national human and animal health experts and as a forum for debating recent developments in the area of influenza.

Secondly, the comprehensive training of laboratory personnel in both influenza diagnostics and laboratory quality and biosafety

TABLE 1. ACHIEVEMENTS BY THE FIVE PIP PC
RECIPIENT COUNTRIES IN THE WHO EUROPEAN REGION

	2014	2017
Newly established or improved sentinel influenza surveillance sites	2	5
Developed a national influenza surveillance bulletin	1	3
Consistently ^a reported ILI/ARI ^b data to WHO during the influenza season	3	3
Consistently reported SARI ^c data to WHO during the influenza season	2	4
Consistently reported virological data to WHO during the influenza season	2	3
Shared influenza viruses with WHO	2	3
Scored 100% in the WHO EQAP ^d	1	5
Uploaded genetic sequence data to GISAID ^e	1	2
Held national annual influenza meeting with participation of animal health sector	0	5
Developed guidelines and associated training for outbreak investigation and response	0	5
Developed guidelines and associated training for clinical management of patients with severe forms of influenza	0	5
^a As defined in the PIP PC Implementation Plan 2013–2016, "consistently" means that a country reports most of the weeks during the influenza season(s)		
^b Influenza-like illness and acute respiratory infection		
^c Severe acute respiratory infection		
^d External Quality Assessment Project		
^e Global Initiative on Sharing All Influenza Data		

has enabled national influenza laboratories to enhance testing for seasonal as well as novel influenza viruses, and to ship samples to WHO GISRS, in compliance with international transport regulations, in time for vaccine strain selection. In particular, national influenza laboratories in Armenia, Kyrgyzstan and Tajikistan shared viruses with WHO GISRS. In addition, national influenza laboratories in all five countries scored 100% in the 2017 WHO External Quality Assessment Project on the detection of influenza viruses by polymerase chain reaction assay as a result of their improvements in laboratory capacity. Furthermore, the national influenza laboratories in Armenia and Tajikistan are in the final stages of being formally recognized by WHO, and formal WHO recognition of the national influenza laboratories in Turkmenistan and Uzbekistan is pending the establishment of mechanisms for sharing influenza viruses with

WHO GISRS. The national influenza laboratory in Kyrgyzstan was formally recognized by WHO in 2008 and the activities described here have contributed to maintaining this status.

Thirdly, the five countries have developed national guidelines on outbreak investigation and response and rapid response teams have been trained. The national guidelines include step-wise and standardized approaches to multidisciplinary and intersectoral outbreak investigation and timely response and provide a number of practical tools to be applied in the field. A team of core trainers was trained in all countries to facilitate roll-out of the guidelines and to cascade training down to the subnational level. These guidelines and the corresponding training package are applicable for investigating and responding to any infectious disease outbreak. Such guidelines, as well as training packages to operationalize them, were so far lacking in the five countries. Representatives from the animal health sector also participated in the training in outbreak investigation and response to enhance collaboration at the human–animal interface.

Fourthly, training courses in the clinical management of patients with severe forms of influenza have enhanced the knowledge and capacities of the countries' frontline health care workers. With a view to ensuring sustainability, representatives of educational institutions attended the courses and it is foreseen that the training modules will be included in national postgraduate education curricula in the coming years. The ability to treat patients with severe forms of influenza is vital both during seasonal influenza epidemics, when severely ill patients are admitted to hospital, as well as during a pandemic. In addition, the treatment procedures are also applicable to severe respiratory infections caused by pathogens other than influenza. The treatment procedures introduced through the training courses have been formalized in newly developed or updated clinical management guidelines and, to maximize the number of health care workers trained, training has been delivered as cascade training from national to local hospitals.

Finally, in addition to country-specific work, PIP PC funds have also allowed for an enhancement of regional initiatives, such as the publication of the weekly influenza update Flu News Europe (18) in English and Russian, as well as strengthening of the influenza network in the WHO European Region through, for example, annual influenza meetings.

preparedness in the WHO European Region. The five PIP PC recipient countries have strengthened some of the essential capacities related to detecting and sharing influenza viruses, responding to outbreaks, monitoring epidemics and treating patients. As the work conducted has enhanced public health functions that go beyond influenza, such as outbreak investigation and response, it has contributed to preparedness for health hazards beyond influenza as well as the strengthening of IHR (2005) core capacities. We believe that the progress made can be attributed to: country commitment leveraged by the formal endorsement of the PIP Framework by countries; sustained funding; and the tailored, step-wise and standardized approach to capacity building that is described in this paper.

While certain achievements are already tangible, others are expected to lay the foundation for sustainable influenza surveillance and response systems in the countries. However, the costs of operating national influenza surveillance systems is one of the areas yet to be assessed on and this will support national governments in allocating and prioritizing resources for the continuation of influenza surveillance systems. These are some of the aspects to be addressed in the coming years as the support to the five countries continues under the PIP PC high-level implementation plan (2018–2023).² This continuation of support provides a means to work towards sustainability by institutionalizing mechanisms and systems within the countries, including their use of surveillance outputs to inform public health actions during the influenza season and in their response to the next pandemic.

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CONCLUSION

Between 2014 and 2017, measurable progress has been made towards strengthening seasonal and pandemic influenza

The PIP PC high level implementation plan (2018–2023) is in the final stages of publication at the time of writing.

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